NATIONAL GUIDELINE CLEARINGHOUSE™ (NGC) GUIDELINE SYNTHESIS

DIAGNOSIS AND MANAGEMENT OF PEDIATRIC URINARY TRACT INFECTION (UTI)

Guidelines

1. **Cincinnati Children's Hospital Medical Center (CCHMC)**. Evidence-based care guideline for medical management of first urinary tract infection in children 12 years of age or less. Cincinnati (OH): Cincinnati Children's Hospital Medical Center; 2006 Nov. 23 p. [70 references]
2. **European Association of Urology (EAU)**. Guidelines on the management of urinary and male genital tract infections. In: guidelines on the management of urinary and male genital tract infections. Arnhem, The Netherlands: European Association of Urology (EAU); 2008 Mar. p. 40-52 [69 references]

INTRODUCTION

A direct comparison of the Cincinnati Children's Hospital Medical Center (CCHMC) and European Association of Urology (EAU) recommendations for management of pediatric UTI is provided in the tables, below.

The CCHMC guideline is an update of the 2005 version. In addition to providing recommendations for both the diagnosis and the management of pediatric UTI, CCHMC specifies pediatric populations outside the remit of the guidelines, including children with known immunodeficiencies, children with pre-existing uropathies and/or genitourinary abnormalities, and children requiring intensive care. The EAU guideline is part of a larger volume of guidelines on the management of urinary and male genital tract infections that was first published in 2001.

The tables below provide a side-by-side comparison of key attributes of each guideline, including specific interventions and practices that are addressed. The language used in these tables, particularly that which is used in Table 4, Table 5 and Table 6, is in most cases taken verbatim from the original guidelines:

- Table 1 provides a quick-view glance at the primary interventions considered by each group.
- Table 2 provides a comparison of the overall scope of both guidelines.
- Table 3 provides a comparison of the methodology employed and documented by both groups in developing their guidelines.
- Table 4 provides a comparison of the availability of the full-text guidelines and the implementation tools provided by the guideline groups.

- Table 5 provides a more detailed comparison of the specific recommendations offered by each group for the topics under consideration in this synthesis, including:
    - Diagnosis
        - Clinical Presentation & Indications for Testing
        - Urine Collection and Laboratory Testing
    - Management
        - Determination of Treatment Setting
        - Antibiotic Therapy
        - Imaging Tests
    - Follow-Up/Prevention of Recurrence
    - Education
- Table 6 lists the potential benefits and harms associated with the implementation of each guideline as stated in the original guidelines.
- Table 7 presents the rating schemes used by both groups to rate the level of evidence and the strength of the recommendations.

A summary discussion of the areas of agreement and areas of differences among the guidelines is presented following the content comparison tables.

Abbreviations

- ASB, asymptomatic bacteriuria
- CCHMC, Cincinnati Children's Hospital Medical Center
- CCM, clean catch midstream
- DMSA, dimercaptosuccinic acid
- DTPA, diethylene triamine pentaacetate
- EAU, European Association of Urology
- IV, intravenous
- LE, leukocyte esterase
- LUTI, lower urinary tract infection
- MAG-3, mercaptoacetyltriglycine
- MCUG, micturating cystourethrogram
- MSU, midstream urine
- RNC, radionuclide cystogram
- SMX/TMP, sulfamethoxazole/trimethoprim
- SPA, suprapubic aspiration
- TC-99m, technetium-99m
- US, ultrasound
- UTI, urinary tract infection
- UUTI, upper urinary tract infection
- VCU, voiding cystourethrography
- VCUG, voiding cystourethrogram
- VUR, vesicoureteral reflux

TABLE 1: COMPARISON OF INTERVENTIONS AND PRACTICES CONSIDERED *("✓" indicates topic is addressed)*		
	CCHMC (2006)	**EAU (2008)**

DIAGNOSIS		
Clinical Presentation & Indications for Testing	✓	✓
Urine Collection & Laboratory Testing	✓	✓
MANAGEMENT		
General Management Recommendations	✓	✓
Antibiotic Therapy	✓	✓
Imaging	✓	✓
FOLLOW-UP/PREVENTION OF RECURRENCE	✓	✓
EDUCATION	✓	

TABLE 2: COMPARISON OF SCOPE AND CONTENT	
OBJECTIVE AND SCOPE	
CCHMC (2006)	• To improve the use of appropriate diagnostic criteria • To improve the use of appropriate antibiotic therapy • To improve the use of appropriate imaging studies • To avoid long-term medical problems • To improve parental involvement in decision-making around the management of UTIs • To identify the infants and children at most risk for long-term renal damage
EAU (2008)	To assist urologists and physicians from other medical specialties in their daily practice
TARGET POPULATION	
CCHMC (2006)	• United States • Children 12 years of age or less, with a first presumed or definite episode of UTI These guidelines are <u>not</u> intended for use in children: • With known immunodeficiencies • With known major genitourinary anomalies

	• With sepsis with shock or meningitis • Needing ventilator or other intensive care • With other severe comorbid conditions
EAU (2008)	Children with UTIs
INTENDED USERS	
CCHMC (2006)	Advanced Practice Nurses Allied Health Personnel Health Care Providers Nurses Patients Physician Assistants Physicians
EAU (2008)	Physician Assistants Physicians

TABLE 3: COMPARISON OF METHODOLOGY		
	CCHMC (2006)	**EAU (2008)**
Methods Used to Collect/Select the Evidence	• *Searches of Electronic Databases* *Described Process:* To select evidence for critical appraisal by the group, the Medline, EmBase, and the Cochrane databases were searched for dates of January 1999 through October 2004 to generate an unrefined, "combined evidence" database using a search strategy focused on answering clinical questions relevant to UTI and employing a combination of Boolean searching on human-indexed thesaurus terms	• *Hand Searches of Published Literature (Primary Sources)* • *Searches of Electronic Databases* *Described Process:* For literature review, PubMed was searched for published meta-analyses, which were used as far as available. Otherwise there was a non-structured literature review process by the group members. Each member was responsible for one

	(Medical Subject Heading [MeSH] headings using an OVID Medline interface) and "natural language" searching on words in the title, abstract, and indexing terms. The citations were reduced by eliminating duplicates, review articles, non-English articles, and adult articles. The resulting abstracts were reviewed by a methodologist to eliminate low-quality and irrelevant citations. During the course of the guideline development, additional clinical questions were generated and subjected to the search process. **November 2006 Update** A search using the above criteria was conducted for dates of October, 2004 through July, 2006. One relevant article was selected as potentially requiring changes to the 2005 version of the recommendations. The article was appraised and the Team approved the changes to the guideline (see the "Development Process" section in the original guideline document for details). *Number of Source Documents:* 669 (2005 version) plus 148 (2006 update) *Number of References:*	chapter (reporter). *Number of Source Documents:* Not stated *Number of References:* 69

	70	
Methods Used to Assess the Quality and Strength of the Evidence	*Not stated*	*Weighting According to a Rating Scheme (Scheme Given - Refer to Table 7)*
Methods Used to Analyze the Evidence	• *Review* • *Review of Published Meta-Analyses* *(Process not described)*	• *Review of Published Meta-Analyses* • *Systematic Review* *Described Process:* The method currently in use ensures that nearly all randomized controlled trials and meta-analyses are included in the guidelines
Methods Used to Formulate the Recommendations	*Expert Consensus* *Described Process:* The recommendations contained in this document were formulated by an interdisciplinary working group which performed systematic and critical literature reviews, using the grading scale described below under "Type of Evidence Supporting the Recommendations," and examined current local practices. Recommendations have been formulated by a consensus process directed by best evidence, patient and family preference, and clinical expertise. During formulation of these guidelines, the team members have remained	*Expert Consensus (Consensus Development Conference)* *Described Process:* The members of the UTI Working Group of the European Association of Urologists (EAU) Health Care Office established the first version of these guidelines in several consensus conferences. The members of the current UTI Working Group of the EAU Guidelines Office updated the guidelines in several consensus conferences thereafter. The first draft of each chapter was sent to the committee members asking for comments, which were then considered, discussed and incorporated accordingly.

	cognizant of controversies and disagreements over the management of these patients. They have tried to resolve controversial issues by consensus where possible and, when not possible, to offer optional approaches to care in the form of information that includes best supporting evidence of efficacy for alternative choices.	The formal agreement to each updated chapter was achieved by the European Association of Urology (EAU) working group at three plenary meetings: the first in Paris on 10 December 2004, the next in Istanbul on 15 March 2005, and finally in Florence on 22 October 2005. Each chapter was reviewed by three committee members (editorial group) for consistency and compatibility in two editorial meetings: one meeting took place in Straubing, 22-24 April 2005, and one in Stavern, 9-11 Sept 2005, and the chapters were revised accordingly.
Outcomes Considered	• Sensitivity and specificity of laboratory testing (urinalysis) • Identification of anatomic abnormalities • Infection recurrence • Long-term renal damage	• Sensitivity and specificity of diagnostic tests • Side effects of treatment • Recurrence rate • Morbidity (renal damage) from UTIs • Correction of association urological lesions
Financial Disclosures/Conflicts of Interest	This guideline was developed without external funding. All Team Members and Clinical Effectiveness support staff listed have declared whether they have any conflict of interest and none were identified.	All members of the Management of Urinary and Male Genital Tract Infections guidelines writing panel have provided disclosure statements of all relationships which they have and which may be perceived as a

		potential source of conflict of interest. This information is kept on file in the European Association of Urology (EAU) Central Office database. This guidelines document was developed with the financial support of the EAU. The EAU is a non-profit organisation and funding is limited to administrative assistance, travel, and meeting expenses. No honoraria or other reimbursements have been provided.

TABLE 4: AVAILABILITY AND IMPLEMENTATION TOOLS PROVIDED	
Composition of Group that Authored the Guideline	
CCHMC (2006)	*Members identified; Affiliations provided; Multidisciplinary; Includes patient representation*
EAU (2008)	*Members identified*
Source(s) of Funding	
CCHMC (2006)	Cincinnati Children's Hospital Medical Center
EAU (2008)	European Association of Urology
Guideline Availability	
CCHMC (2006)	*Electronic and print distribution; Open access* Electronic copies: Available from the Cincinnati Children's Hospital Medical Center Web site. For information regarding the full-text guideline, print copies, or

	evidence-based practice support services contact the Children's Hospital Medical Center Health Policy and Clinical Effectiveness Department at HPCEInfo@chmcc.org.
EAU (2008)	*Electronic and print distribution; Open access* Electronic copies: Available in Portable Document Format (PDF) from the European Association of Urology Web site. Print copies: Available from the European Association of Urology, PO Box 30016, NL-6803, AA ARNHEM, The Netherlands.
Implementation Tools	
CCHMC (2006)	Chart Documentation/Checklists/Forms Clinical Algorithm Foreign Language Translations Patient Resources Quick Reference Guides/Physician Guides
EAU (2008)	Clinical Algorithm Pocket Guide/Reference Cards

TABLE 5: COMPARISON OF RECOMMENDATIONS FOR MANAGEMENT OF PEDIATRIC UTI	
DIAGNOSIS	
Clinical Presentation & Indications for Testing	
CCHMC (2006)	**Assessment and Diagnosis** **History and Physical Examination** It is recommended that prompt evaluation for a diagnosis of UTI be conducted. See Appendix 5 of the original guideline document (reproduced below) for clinical findings consistent with the diagnosis of a UTI. **Note**: Risk factors for UTI include: • Male • Uncircumcised < 1 year • All < 6 months • Female, in general • Particularly < 1 year

	• Non-African-American race • Fever > 39° C *(Shaw 1998 [C], Craig 1996 [C], Hoberman 1993 [C], Bachur 2001a [D], Bachur 2001b [D]).* Absence of high fever or other specific risk factors does not preclude the presence of UTI. See Appendix 2 and Appendix 3 in the original guideline document. **Clinical Signs and Symptoms of UTI** *Newborns* • Jaundice • Sepsis • Failure to thrive • Vomiting • Fever *Infants and Preschoolers* • Diarrhea • Failure to thrive • Vomiting • Fever • Strong-smelling urine • Abdominal or flank pain • New onset urinary incontinence • Dysuria (preschoolers) • Urgency (preschoolers) *School Age Children* • Vomiting • Fever • Strong-smelling urine • Abdominal or flank pain • New onset urinary incontinence • Dysuria • Urgency • Frequency
EAU (2008)	**Signs and Symptoms** Symptoms are non-specific, and vary with the age of the child and the severity of the disease. Epididymo-orchitis is extremely unusual. With scrotal pain and inflammation in a boy, testicular torsion has to be

considered.

A UTI in neonates may be non-specific and with no localization. In small children, a UTI may present with gastrointestinal signs, such as vomiting and diarrhoea. In the first weeks of life, 13.6% of patients with fever have a UTI. Rarely, septic shock will be the presentation. Signs of a UTI may be vague in small children, but later on, when they are older than 2 years, frequent voiding, dysuria and suprapubic, abdominal or lumbar pain may appear with or without fever.

Classification

UTIs may be classified either as a first episode or recurrent, or according to severity (simple or severe).

Recurrent UTI may be subclassified into three groups:

- *Unresolved infection*: subtherapeutic level of antimicrobial, non-compliance with treatment, malabsorption, resistant pathogens.
- *Bacterial persistence*: may be due to a nidus for persistent infection in the urinary tract. Surgical correction or medical treatment for urinary dysfunction may be needed.
- *Reinfection*: each episode is a new infection acquired from periurethral, perineal or rectal flora.

From the clinical point of view, severe and simple forms of UTIs should be differentiated because to some extent the severity of symptoms dictates the degree of urgency with which investigation and treatment are to be undertaken.

Severe UTI

- Fever $\geq$39°C
- Persistent vomiting
- Serious dehydration
- Poor treatment compliance

Severe UTI is related to the presence of fever of > 39°C, the feeling of being ill, persistent vomiting, and moderate or severe dehydration.

Simple UTI

- Mild pyrexia
- Good fluid intake
- Slight dehydration
- Good treatment compliance

A child with a simple UTI may have only mild pyrexia, but is able to take fluids and oral medication. The child is only slightly or not dehydrated and has a good expected level of compliance. When a low

	level of compliance is expected, such a child should be managed as one with a severe UTI. **<u>Diagnosis</u>** **Physical Examination** It is mandatory to look for phimosis, labial adhesion, signs of pyelonephritis, epididymo-orchitis, and stigmata of spina bifida, e.g., hairy patch on the sacral skin. The absence of fever does not exclude the presence of an infective process.
Urine Collection and Laboratory Testing	
CCHMC (2006)	**Laboratory Studies** • It is recommended that urine samples be collected by catheter or SPA (if age-appropriate), if a high quality CCM urine sample cannot be obtained *(Hoberman 1996 [C], Weinberg 1991 [D])*. **Note 1**: In a child with a low clinical suspicion of UTI, and in whom a catheterization would be both required for a culture and considered invasive by the clinician or the family, the option to perform a dipstick or routine urinalysis on a specimen collected by more convenient means may be considered, followed by catheterization if the urinalysis suggests a UTI (*AAP 1999 [S]*). See Table 1 in the original guideline document. **Note 2**: See CCHMC Nursing Policies, Procedures and Standards: "III-701 Urinary Catheterization/Bladder Irrigation" in the "Availability of Companion Documents" field. • It is recommended, in screening for UTI, to perform: • Dipstick (nitrite and LE) **or** • Routine urinalysis (nitrite, LE and microscopy) **And** • Urine culture and susceptibilities *(Gorelick 1999 [M])*. See Table 1 in the original guideline document. **Note**: Gram stain is not commonly conducted in the Cincinnati pediatric community *(Hoberman 1996 [C])*. **Diagnosis** *General* <u>Presumed UTI</u> is diagnosed while urine culture results are pending in a

	child with abnormal laboratory studies and clinical findings consistent with the diagnosis of a UTI. Definite UTI is diagnosed after obtaining a positive result for a urine culture in a child presenting with a clinical profile consistent with a UTI. *Presumed UTI* It is recommended that while pending results of culture, any positive result from a dipstick or routine urinalysis, in the presence of clinical findings consistent with the diagnosis of a UTI, be considered consistent with a presumptive diagnosis of UTI *(Gorelick 1999 [M])*. Any one of the following study results defines a positive urinalysis *(Gorelick 1999 [M])*. See Table 1 and Table 2 in the original guideline document. • Positive nitrite screen • Positive LE • Positive microscopic exam: the definition of abnormal microscopic exam is dependent on patient or provider-specific determinants *Definite UTI* It is recommended that a definite UTI be defined as a single organism cultured from a SPA, catheter specimen, or CCM specimen at the following concentrations. The higher the concentration of organisms, the more reliable the results; however, colony counts must be interpreted within the clinical context and lower colony counts may be significant, especially in a dilute urine • SPA: > 1,000 cfu/mL • Cath: > 10,000 cfu/mL • CCM: > 100,000 cfu/mL *(Hansson 1998 [C], Rushton 1997 [S,E])*
EAU (2008)	**Diagnosis** **Laboratory Tests** The definitive diagnosis of infection in children requires a positive urine culture. Urine must be obtained under bacteriologically reliable conditions when undertaking a urine specimen culture. A positive urine culture is defined as the presence of more than 100,000 cfu/mL of one pathogen. The urine specimen may be difficult to obtain in a child less than 4 years old and different methods are advised since there is a high risk of contamination.

Collection of the Urine

Suprapubic Bladder Aspiration

Suprapubic bladder aspiration is the most sensitive method, even though urine may be obtained in 23-99% of cases.

Bladder Catheterization

Bladder catheterization is also a most sensitive method, even though there is the risk of introduction of nosocomial pathogens.

Plastic Bag Attached to the Genitalia

Prospective studies showed a high incidence of false-positive results, ranging from 85-99%. It is helpful when the culture is negative and has a positive predictive value of 15%. In order to obtain a urine sample in the best condition in children under 2 years of age (girls and uncircumcised boys without sphincteric control), it is better to use suprapubic bladder aspiration or bladder catheterization. In older children with sphincteric control, MSU collection is possible and reliable.

Quantification of Bacteriuria

The final concentration of bacteria in urine is directly related to the method of collection, diuresis, method of storage and transport of the specimen. The classical definition of significant bacteriuria of more than 10^5 cfu/mL is still used and depends on the clinical environment.

The presence of pyuria (more than 5 leucocytes per field) and bacteriuria in a fresh urine sample will reinforce the clinical diagnosis of UTI.

In boys, when the urine is obtained by bladder catheterization, the urine culture is considered positive with more than 10^4 cfu/mL. Even though Hoberman identified a micro-organism in 65% of cases with colony counts between 10,000 and 50,000 cfu/mL, there was a mixed growth pattern suggesting contamination. In these cases, it is better to repeat the culture or to evaluate the presence of other signs, such as pyuria, nitrites or other biochemical markers. The collection of MSU or in a collecting bag of more than 10^5 cfu/mL is considered positive.

Criteria of UTI in Children

Urine specimen from SPA: Any number of cfu/mL (at least 10 identical colonies)

Urine specimen from bladder catheterization: $\geq$ 1,000-50,000

cfu/mL

Urine specimen from midstream void: $\geq 10^4$ cfu/mL with symptoms; $\geq 10^5$ cfu/mL without symptoms

Other Biochemical Markers

The presence of other biochemical markers in a urine sample are useful to establish the diagnosis of UTI. The most frequent markers are nitrite and LE usually combined in a dipstick test.

The dipstick test has become useful to exclude rapidly and reliably the presence of a UTI, provided both nitrite and LE tests are negative. If the tests are positive, it is better to confirm the results in combination with the clinical symptoms and other tests.

Bacteriuria without pyuria may be found:

- In bacterial contamination
- In colonization (asymptomatic bacteriuria)
- When collecting a specimen before the onset of an inflammatory reaction

In such cases, it is advisable to repeat the urinalysis after 24 hours to clarify the situation. Even in febrile children with a positive urine culture, the absence of pyuria may cast doubt on the diagnosis of UTI. Instead, asymptomatic bacteriuria with a concomitant septic focus responsible for the febrile syndrome has to be considered.

Bacteriuria without pyuria is found in 0.5% of specimens. This figure corresponds well with the estimated rate of asymptomatic bacteriuria in childhood **(IIa)**.

Pyuria without bacteriuria may be due to:

- Incomplete antimicrobial treatment of UTI
- Urolithiasis and foreign bodies
- Infections caused by *Mycobacterium tuberculosis* and other fastidious bacteria, e.g., *Chlamydia trachomatis*.

Thus, either bacteriuria or pyuria may not be considered reliable parameters to diagnose or exclude UTI. Their assessment can be influenced by other factors, such as the degree of hydration, method of specimen collection, mode of centrifugation, volume in which sediment is resuspended and subjective interpretation of results. However, according to Landau et al., pyuria in febrile children is indicative of acute pyelonephritis.

For all of these reasons, in neonates and children under 6 months of age, either pyuria, bacteriuria or the nitrite test, separately, have

	minimal predictive value for UTI **(III)**. In contrast, the positive predictive value of significant Gram staining with pyuria is 85% **(IIb)**. In older children, pyuria with a positive nitrite test is more reliable for the diagnosis of UTI, with a positive predictive value of 98%. Combining bacteriuria and pyuria in febrile children, the findings of > 10 WBC/mm^3 and > 50,000 cfu/mL in a specimen collected by catheterization are significant for a UTI and discriminate between infection and contamination. *C-reactive Protein* Although non-specific in febrile children with bacteriuria, C-reactive protein seems to be useful in distinguishing between acute pyelonephritis and other causes of bacteriuria. It is considered significant at a concentration above 20 microg/mL. *Urinary N-acetyl-β-glucosaminidase* This is a marker of tubular damage. It is increased in a febrile UTI and may become a reliable diagnostic test for UTIs, although it is also elevated in VUR. *Interleukin-6* The clinical use of urinary concentrations of interleukin-6 in UTIs is still at the research stage.
MANAGEMENT	
Determination of Treatment Setting	
CCHMC (2006)	**Admission Criteria** It is recommended that admission be primarily restricted to infants and children: • Who require IV for fluids • Who require IV antibiotics due to severe illness or due to lack of response to by mouth (PO) antibiotics **Note**: A high quality, randomized controlled trial demonstrated that oral cefixime is a safe and effective treatment for children age 1 to 24 months with definite UTI *(Hoberman 1999 [A])*. • Who are 0 to 30 days of age • Who are 31 to 60 days of age and identified as high-risk clinically or by laboratory data • With whom the clinician or family is uncomfortable managing in an

	outpatient setting *(Local Expert Consensus, [E])* **Discharge Criteria** It is recommended that the hospitalized child be discharged as soon as: • Afebrile for at least 12 hours • Taking adequate oral fluids • Pain controlled with oral medications • Home antibiotics tolerated (PICC line or oral) • Parent confident in caring for child at home • Imaging studies are complete or arrangements have been made • Primary care provider(s) identified, notified, and agree(s) with discharge decision, and arrangements for appropriate follow up have been made *(Local Expert Consensus [E])*
EAU (2008)	*Electronic and print distribution; Open access* If the child is severely ill with vomiting and dehydration, hospital admission is required and parenteral antibiotics are given initially **(A)**. For a safety period of 24-36 hours, parenteral therapy should be administered. When the child becomes afebrile and is able to take fluids, he/she may be given an oral agent to complete the 10-14 days of treatment, which may be continued on an outpatient basis. This provides some advantages, such as less psychological impact on the child and more comfort for the whole family. It is also less expensive, well tolerated and eventually prevents opportunistic infections.
Antibiotic Therapy	
CCHMC (2006)	**Medications** • It is recommended that a child with presumed UTI be empirically treated with antibiotics after obtaining an appropriate sample for culture. Prompt treatment with antibiotics reduces the severity of renal scarring *(Benador 1997 [C], Winberg 1982 [S,E])*. See Appendix 7 and Appendix 8 of the original guideline document for summary of recommended doses for parenteral and oral antibiotics, respectively. **Note:** Well-appearing children who are not febrile, and in whom dipstick or urinalysis results are equivocal, can be considered for outpatient observation without starting antibiotic therapy until the subsequent clinical course and culture results are known. As long

as uncertainty persists, this course of management assumes:

- Available reliable follow up as needed
- Healthcare provider(s) confident that caregiver will use appropriate observational and follow-up skills

(Local Expert Consensus, [E])

- It is recommended, if the child is diagnosed with a definite UTI, that antibiotic therapy be continued for a minimum of 7 to 14 days *(Keren 2002 [M])*. Culture and susceptibility results may indicate that a change of antibiotic is necessary. See Appendix 7 and Appendix 8 in the original guideline document for summary of recommended doses for parenteral and oral antibiotics, respectively.
- It is recommended, if the urine culture is negative, that antibiotics be discontinued *(Local Expert Consensus [E])*.

Follow-Up

- It is recommended, for children who will have imaging, to consider the use of post-treatment antibiotic prophylaxis until radiologic evaluation results are known (Local Expert Consensus, [E]). See Appendix 11 in the original guideline document for a summary of recommended doses of prophylactic antibiotics.

  Note: Uncertainty exists regarding the effectiveness of prophylaxis in improving outcomes *(Garin et al., 2006, [A]; Beetz, 2006 [S])*. See Appendix 12 in the original guideline document for further information on UTI prophylaxis.

NGC Note: The antibiotics listed below are taken from Appendices 7, 8 and 11 of the original guideline document. Refer to these appendices in the original guideline document for information regarding: dose, frequency and maximum daily dose; taste; relative cost; and comments.

Parenteral Antibiotics for Treatment of UTI (usually inpatient)

- Cefotaxime (Claforan®)
- Ampicillin
- Gentamicin
- Ceftriaxone (Rocephin®)

Antibiotics for Outpatient Treatment of UTI

Recommend minimum of 7 to 14 days treatment.

First-Line Antibiotics Recommended for First UTI

	• Cefixime (Suprax®) • Cephalexin (Biocef®, Keflex®) • Sulfamethoxazole/Trimethoprim (Bactrim®, Septra®, Generic) *Alternative Antibiotics for Patients with Special Circumstances* • Nitrofurantoin (Macrodantin®, Furadantin®) • Ciprofloxacin (Cipro®) • Ceftriaxone (Rocephin®) **Prophylactic Antibiotics** Recommend until radiologic evaluation results are known and duration individualized thereafter. • Sulfamethoxazole/Trimethoprim (Bactrim®, Septra®, Generic) • Nitrofurantoin (Macrodantin®, Furadantin®) • Amoxicillin • Cephalexin (Biocef®, Keflex®)
EAU (2008)	**Summary and Recommendations** In the treatment of a UTI in children, short courses are not advised and therefore treatment is continued for 5-7 days and longer **(A)**. If the child is severely ill with vomiting and dehydration, hospital admission is required and parenteral antibiotics are given initially **(A)**. **Treatment** **Severe UTIs** A severe UTI requires adequate parenteral fluid replacement and appropriate antimicrobial treatment, preferably with cephalosporins (third generation). If a Gram-positive UTI is suspected by Gram stain, it is useful to administer aminoglycosides in combination with ampicillin or amoxycillin/clavulanate **(IIa)**. Antimicrobial treatment has to be initiated on an empirical basis, but should be adjusted according to culture results as soon as possible. In patients with an allergy to cephalosporins, aztreonam or gentamicin may be used. When aminoglycosides are necessary, serum levels should be monitored for dose adjustment. Chloramphenicol, sulphonamides, tetracyclines, rifampicin, amphotericin B and quinolones should be avoided. The use of ceftriaxone must also be avoided due to its undesired side effect of jaundice. A wide variety of antimicrobials can be used in older children, with the exception of tetracyclines (because of teeth staining). Fluorinated

	quinolones may produce cartilage toxicity, but if necessary may be used as second-line therapy in the treatment of serious infections, since musculoskeletal adverse events are of moderate intensity and transient. For a safety period of 24-36 hours, parenteral therapy should be administered. When the child becomes afebrile and is able to take fluids, he/she may be given an oral agent to complete the 10-14 days of treatment, which may be continued on an outpatient basis. This provides some advantages, such as less psychological impact on the child and more comfort for the whole family. It is also less expensive, well tolerated and eventually prevents opportunistic infections. The preferred oral antimicrobials are: TMP, co-trimoxazole (TMP plus sulphamethoxazole), an oral cephalosporin, or amoxycillin/clavulanate. However, the indication for TMP is declining in areas with increasing resistance. In children less than 3 years of age, who have difficulty taking oral medications, parenteral treatment for 7-10 days seems advisable, with similar results to those with oral treatment. If there are significant abnormalities in the urinary tract (e.g., VUR, obstruction), appropriate urological intervention should be considered. If renal scarring is detected, the patient will need careful follow-up by a paediatrician in anticipation of sequelae such as hypertension, renal function impairment and recurrent UTI. An overview of the treatment of febrile UTIs in children is given in Figure 3.2 of the original guideline document and the dosing of antimicrobial agents is outlined in Table 3.3 in the original guideline document. **Simple UTIs** A simple UTI is considered to be a low-risk infection in children. Oral empirical treatment with TMP, an oral cephalosporin or amoxycillin/clavulanate is recommended, according to the local resistance pattern. The duration of treatment in uncomplicated UTIs treated orally should be 5-7 days **(Ib)**. A single parenteral dose may be used in cases of doubtful compliance and with a normal urinary tract **(IIa)**. If the response is poor or complications develop, the child must be admitted to hospital for parenteral treatment. **Prophylaxis** If there is an increased risk of pyelonephritis, e.g., VUR, and recurrent UTI, low-dose antibiotic prophylaxis is recommended **(IIa)**. It may also be used after an acute episode of UTI until the diagnostic work-up is completed. The most effective antimicrobial agents are: nitrofurantoin, TMP, cephalexin and cefaclor.
Imaging Tests	

CCHMC (2006)	**Imaging** Imaging procedures available for children with UTI are described in Appendix 9 of the original guideline document: ultrasound (US), cystogram and renal cortical scan. See also imaging algorithm, page 8 and Appendix 10 (reflux grading system) of the original guideline document. A primary goal of imaging is to identify structural abnormalities of the urinary tract or bladder that may benefit from surgical or medical intervention. Decisions to perform imaging presume that the findings will sufficiently influence management to justify the burden of testing; for example, the discomfort of catheterization. **Note 1**: The diagnostic validity of a cystogram for detection of VUR does not appear to be affected if the procedure is performed during an inpatient stay for treatment of UTI *(Mahant 2001 [D])*. **Note 2**: Routine cystogram and US following a first childhood UTI identifies a small proportion of children with associated treatable conditions. The approximate prevalences of VUR among girls age 0 to 18yrs referred for VCUG after documented UTI (first or subsequent) are: Grade I 7%; Grade II 22%; Grade III 6%; Grade IV 1%; and Grade V <1% *(Bisset 1987 [D])*. The prevalence of US-identified anatomic abnormalities amenable to surgical correction following first UTI is approximately 1% *(Zamir 2004 [C], Bisset 1987 [D])*. • It is recommended, because careful long-term outcomes research has not been performed, that children in the following categories, with a first UTI, have a cystogram and US. See Appendix 9 in the original guideline document. • All boys • Girls age < 36 months (see Note 1 below) • Girls age 3 to 7 years (84 months) **with fever** > 38.5° C (101.3° F) *(Gordon 2003 [M], Hoberman 2003 [A], Wennerstrom 2000b [C], Jodal 2000 [S], AAP 1999 [S]).* **Note 1**: Although an age break at three years is used, the appropriate age cutoff may depend, in part, on the girl's ability to verbalize dysuria symptoms and/or her status of toilet training *(Local Expert Consensus [E])*. **Note 2**: A relatively small number of significant anatomic abnormalities will be missed if routine imaging after first UTI is not done *(Zamir 2004 [C], Bisset 1987 [D])*.

Note 3: Schedule the US and cystogram for the same date, with the cystogram to follow the US. If an RNC has been ordered, and if there are significant US abnormalities, the Radiology staff physician will ask to substitute a VCUG for the RNC at that appointment *(Local Expert Consensus, [E])*.

Note 4: An optional imaging evaluation for children with febrile UTI, especially those over age three years is to first perform US and renal cortical scan (see Appendix 9). This avoids bladder catheterization (part of the cystogram procedure) if the results of the scan are normal. However, if pyelonephritis or cortical scarring is found on the renal cortical scan, a cystogram is indicated *(Local Expert Consensus, [E])*.

- It is recommended, for children in the following categories, that observation without imaging be considered and that the family share in the decision of whether or not imaging be performed after the first UTI or delayed until after the second UTI, if one occurs:
    - Girls $\geq$3 years of age without fever (temperature >38.5 degrees C)
    - All girls >7 years of age

(Local Expert Consensus, [E])

Observation without imaging is defined as follow-up with dipstick or routine urinalysis when age-appropriate symptoms of UTI are observed.

Note 1: For imaging after first or second UTI, one option is to perform a cystogram and US. An alternative, for febrile UTI, is to perform a renal cortical scan and US (see Note 4 in the previous recommendation, and see Appendix 9 in the original guideline document).

Note 2: Factors influencing choice of imaging option:

- Clinical symptoms and rate of resolution (see Appendix 5 in the original guideline document)
- Age (continuously decreasing risk of reflux over age 5 years)
- Abnormal relevant history (e.g., voiding dysfunction) or physical exam (e.g., sacral dimple)
- Family input: family understands the imaging procedures, that there is a small chance that an anatomic abnormality exists, and that close follow-up is needed for subsequent UTIs after which imaging may be performed
- Compliance: confidence that caregiver will use appropriate observational skills and follow-up
- African-Americans have lower risk of VUR and renal damage *(West & Venugopal, 1993 [C]; Chand et al., 2003 [D];*

	Melhem & Harpen, 1997 [D]; Askari & Belman, 1982 [D]) • Availability of prenatal US images for review by radiologist *(Ismaili et al., 2004 [C]; Chitty et al., 1991 [D])* • It is recommended that a renal cortical scan be considered if identification of acute pyelonephritis or renal scarring will affect management decisions in febrile UTI *(Wennerstrom et al., "Ambulatory blood pressure," 2000 [C]; Wennerstrom et al., "Renal function," 2000 [C]; Majd & Rushton, 1992 [S, E]; Rushton et al., 1988 [F]).* See Appendix 9 in the original guideline document. **Note**: The long-term significance of scarring identified by a renal cortical scan remains unclear. Factors to be considered are illness severity, grade of VUR, radiation exposure, and avoidance of bladder catheterization.
EAU (2008)	**Summary and Recommendations** Investigations should be undertaken after a maximum of two episodes of a UTI in girls and one in boys **(B)**. The objective is to rule out the unusual occurrence of obstruction, VUR and dysfunctional voiding, e.g., as caused by a neuropathic disorder. **Imaging of the Urinary Tract** A 'gold standard' imaging technique has to be cost-effective, painless, safe, with minimal or nil radiation, and an ability to detect any significant structural anomaly. Current techniques do not fulfill all such requirements. <u>Ultrasonography</u> US has become very useful in children because of its safety, speed and high accuracy in identifying the anatomy and size of the renal parenchyma and collecting system. It is subjective and therefore operator-dependent, and gives no information on renal function. However, scars can be identified, although not as well as with Tc-99m DMSA scanning **(IIa)**. This technique has been shown to be very sensitive and excretory urography must be reserved only for when images need to be morphologically clarified **(IIa)**. <u>Radionuclide Studies</u> Tc-99m DMSA is a radiopharmaceutical that is bound to the basement membrane of proximal renal tubular cells; half of the dose remains in the renal cortex after 6 hours. This technique is helpful in determining functional renal mass and ensures an accurate diagnosis of cortical scarring by showing areas of hypoactivity indicating lack of function. A UTI interferes with the uptake of this radiotracer by the proximal renal

tubular cells, and may show areas of focal defect in the renal parenchyma. A star-shaped defect in the renal parenchyma may indicate an acute episode of pyelonephritis. A focal defect in the renal cortex usually indicates a chronic lesion or a 'renal scar' **(IIa)**.

A focal scarring or a smooth uniform loss of renal substance as demonstrated by Tc-99m DMSA has generally been regarded as being associated with VUR (reflux nephropathy). However, Rushton et al. stated that significant renal scarring may develop, regardless of the existence or absence of VUR. Ransley and Risdon reported that Tc-99m DMSA showed a specificity of 100% and sensitivity of 80% for renal scarring.

The use of Tc-99m DMSA scans can be helpful in the early diagnosis of acute pyelonephritis. About 50-85% of children will show positive findings in the first week. Minimal parenchymal defects, when characterized by a slight area of hypoactivity, can resolve with antimicrobial therapy. However, defects lasting longer than 5 months are considered to be renal scarring **(IIa)**.

Tc-99m DMSA scans are considered more sensitive than excretory urography and ultrasonography in the detection of renal scars. It remains questionable whether radionuclide scans could substitute for echography as a first-line diagnostic approach in children with a UTI.

<u>Cystourethrography</u>

Conventional VCU

VCU is the most widely used radiological exploration for the study of the lower urinary tract and especially of VUR. It is considered mandatory in the evaluation of UTIs in children less than 1 year of age. Its main drawbacks are the risk of infection, the need for retrogrades filling of the bladder and the possible deleterious effect of radiation on children. In recent years, tailored low-dose fluoroscopic VCU has been used for the evaluation of VUR in girls in order to minimize radiological exposure. VCU is mandatory in the assessment of febrile childhood UTI, even in the presence of normal ultrasonography. Up to 23% of these patients may reveal VUR.

Radionuclide Cystography (Indirect)

This investigation is performed by prolonging the period of scanning after the injection of Tc-99m DTPA or MAG-3 as part of a dynamic renography. It represents an attractive alternative to conventional cystography, especially when following patients with reflux, because of its lower dose of radiation. Disadvantages are a poor image resolution and difficulty in detecting lower urinary tract abnormalities.

	Cystosonography Contrast material-enhanced voiding ultrasonography has been introduced for the diagnoses of VUR without irradiation. Further studies are necessary to determine the role of this new imaging modality in UTI. <u>Additional Imaging</u> Excretory urography remains a valuable tool in the evaluation of the urinary tract in children, but its use in UTIs is debatable unless preliminary imaging has demonstrated abnormalities requiring further investigation. <u>Urodynamic Evaluation</u> When voiding dysfunction is suspected, e.g., incontinence, residual urine, increased bladder wall thickness, urodynamic evaluation with uroflowmetry, (video) cystometry, including pressure flow studies, and electromyography should be considered. **<u>Schedule of Investigation</u>** Screening of infants for asymptomatic bacteriuria is unlikely to prevent pyelonephritic scar formation, as these usually develop very early in infancy. Only a minority of children with a UTI have an underlying urological disorder, but when present such a disorder can cause considerable morbidity. Thus, after a maximum of two UTI episodes in a girl and one episode in a boy, investigations should be undertaken (Figure 3.1 in the original guideline document), but not in the case of asymptomatic bacteriuria. The need for DTPA/MAG-3 scanning is determined by the ultrasound findings, particularly if there is suspicion of an obstructive lesion.
FOLLOW-UP/PREVENTION OF RECURRENCE	
CCHMC (2006)	**Follow-up** • It is not recommended that routine follow-up urine cultures be conducted during the initial course of inpatient or outpatient therapy. **Note**: In a retrospective study, there were no positive results among follow-up urine cultures in 291 children while hospitalized with UTI. Thirty-two percent of these patients had fever longer than 48 hours *(Currie et al., 2003 [D])*. • It is recommended that follow-up assessment for expected clinical response occur after 48 to 72 hours of antimicrobial therapy. Culture and susceptibility results may indicate that a change of

	antibiotic is necessary. If expected clinical improvement is lacking, consider further evaluation which may include laboratory studies, imaging, and/or consultation with specialists *(Local Expert Consensus, [E])*. • It is recommended that families and clinicians maintain a high index of suspicion for recurrent UTI, and to obtain a dipstick, urinalysis, and/or culture for age-appropriate symptoms of UTI, including unexplained fever *(Wennerstrom et al., "Ambulatory blood pressure," [C]; Local Expert Consensus, [E]). See Table above titled "Clinical Signs and Symptoms of UTI".* Screening urine cultures are not necessary *(Wettergren et al., 1990, [C])*. **Note**: Low rates of scarring, **hypertension**, and loss of renal function have been attributed to aggressive assessment of febrile illnesses and treatment of recurrent UTI *(Wennerstrom et al., "Ambulatory blood pressure," [C]; Wennerstrom et al., "Renal function," 2000 [C]; Wennerstrom et al., "Primary and acquired," 2000 [C])*. • It is recommended, for children who will have imaging, to consider the use of post-treatment antibiotic prophylaxis until radiologic evaluation results are known *(Local Expert Consensus, [E])*. See appendix 11 in the original guideline document for a summary of recommended doses of prophylactic antibiotics. **Note**: Uncertainty exists regarding the effectiveness of prophylaxis in improving outcomes *(Garin et al., 2006, [A]; Beetz, 2006 [S])*. See Appendix 12 in the original guideline document for further information on UTI prophylaxis. **Consults and Referrals** • It is recommended that consultation with a specialist in childhood renal disorders be considered: • When uncertain about the management of a child with documented or suspected vesicoureteral reflux, renal scarring, or structural abnormalities of the urinary tract • If a renal or bladder stone is identified *(Local Expert Consensus, [E])*. • It is recommended that a consultation with Infectious Diseases be considered when there are questions about antibiotic selection or unusual organisms *(Local Expert Consensus, [E])*.
EAU (2008)	**Severe UTIs** If there are significant abnormalities in the urinary tract (e.g., VUR, obstruction), appropriate urological intervention should be considered.

	If renal scarring is detected, the patient will need careful follow-up by a paediatrician in anticipation of sequelae such as hypertension, renal function impairment and recurrent UTI.
EDUCATION	
CCHMC (2006)	**Education** Health Topics on CCHMC's website: • Urine Culture: Adult Assisting a Female Child • Urine Culture: Adult Assisting a Male Child • Vesicoureteral Reflux/VUR Imaging Procedures: • Kidney Ultrasound (US) • Renal Cortical Scan/DMSA A parent information brochure, Urinary Tract Infections in Young Children is available for bulk purchase from the AAP.
EAU (2008)	No recommendations offered.

TABLE 6: BENEFITS AND HARMS	
Benefits	
CCHMC (2006)	• Improved use of appropriate diagnostic criteria • Improved use of appropriate antibiotic therapy • Improved use of appropriate imaging studies • Avoidance of long-term medical problems • Improved parental involvement in decision-making around the management of UTIs • Identification of the infants and children at most risk for long-term renal damage
EAU (2008)	• Cure of UTIs • Reduction in UTI recurrences • Avoidance of long-term medical problems
Harms	

CCHMC (2006)	• Burden of imaging (e.g., discomfort of catheterization, radiation exposure) versus missed identification of treatable anatomic abnormalities • Use of amoxicillin for treatment of the acute UTI may be limited due to increasing resistance. • Ceftriaxone and sulfamethoxazole/trimethoprim should be used with caution in jaundiced infants. • Limitations of radiologic imaging: ultrasound has limited accuracy in evaluation of renal scarring or pyelonephritis; radionuclide cystogram provides little anatomic detail; x-ray voiding cystourethrogram involves ionizing radiation; renal cortical scan requires intravenous injection of radioisotope, with imaging about 2 hours later for about 45 minutes)
EAU (2008)	• Exposure to radiation from diagnostic imaging • Side effects of antibiotics

TABLE 7: EVIDENCE RATING SCHEMES AND REFERENCES

CCHMC (2006)

Cincinnati Children's Hospital and Medical Center Grading Scale

M: Meta-analysis
A: Randomized controlled trial: large sample
B: Randomized controlled trial: small sample
C: Prospective trial or large case series
D: Retrospective analysis
O: Other evidence
S: Review article
E: Expert opinion or consensus
F: Basic laboratory research
L: Legal requirement
Q: Decision analysis
X: No evidence

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EAU (2008)	**Levels of Evidence** **Ia** Evidence obtained from meta-analysis of randomized trials **Ib** Evidence obtained from at least one randomized trial **IIa** Evidence obtained from at least one well-designed controlled study without randomization **IIb** Evidence obtained from at least one other type of well-designed quasi-experimental study **III** Evidence obtained from well-designed non-experimental studies, such as comparative studies, correlation studies and case reports **IV** Evidence obtained from expert committee reports or opinions or clinical experience of respected authorities **Grades of Recommendation** **A** Based on clinical studies of good quality and consistency addressing the specific recommendations and including at least one randomized trial **B** Based on well-conducted clinical studies, but without randomized clinical studies **C** Made despite the absence of directly applicable clinical studies of good quality

GUIDELINE CONTENT COMPARISON

The Cincinnati Children's Hospital Medical Center (CCHMC) and the European Association of Urology (EAU) present recommendations for the diagnosis and

management of pediatric UTI and provide explicit reasoning behind their judgments.

Guideline Development Methodology

To collect and select the evidence, EAU performed hand searches of published literature and both groups performed searches of electronic databases. For the latter process, EAU provides the name of one database that was searched for meta-analyses (PubMed). CCHMC, in contrast, searched three electronic databases (Medline, EmBase and Cochrane) and provides relevant information including dates searched, search strategy used, and exclusion criteria that were applied.

In terms of methods used to assess the quality and strength of the evidence, EAU rated the studies cited from the literature according to the level of evidence and the recommendations were graded accordingly. Both the rating scheme for the levels of evidence and the grading scheme for the guideline recommendations are provided. Although CCHMC does not employ a rating scheme for the strength of evidence, it uses a grading scale to indicate the nature of the evidence (e.g., RCT: large sample, review article, basic laboratory research, etc.) in the reference list as well as in the body of the guideline.

To analyze the evidence, both groups performed a review of published meta-analyses. CCHMC also performed a review, and EAU also performed a systematic review. EAU provides a brief description of processes used to analyze the evidence.

Expert consensus (through use of Consensus Development Conference in the case of EAU) was used by both groups to formulate the recommendations and both provide detailed descriptions of the processes used. CCHMC recommendations were formulated by a consensus process directed by best evidence, patient and family preference, and clinical expertise. EAU recommendations were developed over the course of several working group meetings, during which each chapter was reviewed for consistency and compatibility.

CCHMC provides its guidance in the form of numbered recommendation statements. They link the supporting evidence directly to the recommendation statements and supplement the recommendations with "notes" which provide additional guidance and/or the rationale for the associated recommendation. The EAU guideline provides its guidance primarily in narrative form, with graded recommendation statements found in the "Summary and recommendations" section at the beginning of the guideline. Evidence grades for particular statements are included throughout the guideline, as well as in-text numbers corresponding to the particular evidence in the list of references.

Both groups supply reference lists (70 for CCHMC, 69 for EAU) and present potential conflicts of interest.

Areas of Agreement

Indications for Testing & Clinical Presentation

Both groups agree that symptoms of UTI vary according to age and severity of disease. Both groups provide common symptoms of UTI for children in different age groups: newborns; infants and preschoolers; and school age children (CCHMC) and neonates, small children, and children older than two years (EAU). The groups agree that symptoms indicative of UTI can include: fever, vomiting, failure to thrive, offensive urine, dysuria, urgency, frequency, or changes to continence.

Both groups stress the importance of differentiating between simple and severe forms of UTIs to ensure appropriate subsequent management. Fever $\geq$ 39°C, persistent vomiting, serious dehydration, and poor treatment compliance comprise the symptoms of severe UTI outlined by EAU. Children considered to have severe UTI by CCHMC include those who require IV for fluids or IV antibiotics due to severe illness or due to lack of response to PO antibiotics, who are 0 to 30 days of age, or who are 31 to 60 days of age and identified as high-risk clinically or by laboratory data. Both guidelines emphasize that the absence of fever does not exclude the presence of UTI.

Urine Collection and Laboratory Testing

Both groups agree that a high-quality clean catch urine sample is the preferred method for urine collection. If unobtainable, CCHMC recommends urine samples be collected by catheter or SPA (if age-appropriate). EAU similarly notes that while midstream urine in older children with sphincteric control is recommended, in children under two years of age it is preferable to use SPA or catheter.

Both groups also agree that the definitive diagnosis of UTI in children requires a positive urine culture, defined as the presence of more than 100,000 cfu/mL of one pathogen in a CCM urine sample, or more than 10,000 cfu/mL in a catheter sample (EAU states that the latter figures applies to samples taken from boys; CCHMC does not make this distinction). For SPA, CCHMC defines the presence of more than 1,000 cfu/mL a positive diagnosis; EAU states for SPA it can be any number of cfu/mL, but must be at least 10 identical colonies.

In addition to recommending a culture be performed, both groups also address the use of dipstick testing. CCHMC recommends either dipstick testing or routine urinalysis be performed in addition to culture. EAU does not make a formal recommendation, but notes that the dipstick test has become useful to exclude rapidly and reliably the presence of a UTI, provided both nitrite and LE tests are negative.

Determination of Treatment Setting

The guidelines agree that children who are severely ill with vomiting and dehydration requiring IV for fluids should be managed as inpatients and given parenteral antibiotics. CCHMC also recommends that the following patients be admitted: infants who are 0 to 30 days of age, infants who are 31 to 60 days of age and identified as high-risk clinically or by laboratory data, and infants and children with whom the clinician or family is uncomfortable managing in the outpatient setting.

There is also agreement that discharge can be considered when the patient is afebrile, able to take fluids orally, and able to take oral antibiotics. Both groups agree that oral antibiotic treatment can then be continued on an outpatient basis.

Antibiotic Therapy

The guideline groups are in agreement that empiric antibiotic therapy should be initiated while pending results of culture, and should be discontinued or modified according to culture results.

Both groups provide antibiotic therapy recommendations according to severity of clinical presentation. They are in agreement that parental antibiotic therapy is recommended for inpatient management of severe UTI, and that third generation cephalosporins are the first-line parenteral antibiotic of choice. CCHMC recommends cefotaxime and both groups recommend ceftriaxone. EAU notes, however, that the latter is contraindicated in patients allergic to cephalosporins, due to its undesired side effect of jaundice. CCHMC cautions that ceftriaxone use should be reserved for children unable to tolerate oral route or when compliance is a concern. They add that it should be used with caution in jaundiced infants.

Both groups also address parenteral use of the aminoglycoside gentamicin. EAU notes that if a gram-positive UTI is suspected by gram-stain, it is useful to administer aminoglycosides in combination with ampicillin or amoxicillin/clavulanate. CCHMC similarly notes that gentamicin should not be used as first-line drug monotherapy and should be combined with ampicillin in children 0 to 30 days of age, and should be considered to be combined with ampicillin in children 30 to 60 days of age. EAU also addresses gentamicin in relation to children with allergy to cephalosporins, noting that in this case, gentamicin or aztreonam may be used. CCHMC does not specifically address the issue of cephalosporin allergy.

With regard to oral antibiotics, the groups agree that these should be recommended for management of non-severe, uncomplicated UTI. Both groups recommend SMP/TMX and oral cephalosporins as appropriate first-line oral antibiotics; EAU also recommends amoxicillin-clavulanate. CCHMC provides recommendations for alternative antibiotics for patients with special circumstances.

Recommendations regarding duration of antibiotic therapy for severe UTI are similar. The groups agree that parenteral therapy should begin empirically while awaiting culture results, and that if the culture is positive, therapy should continue to complete a total course of approximately 10 to 14 days. Recommendations regarding the duration of oral antibiotic treatment for non-severe UTI, however, differ. See Areas of Differences below.

The groups agree that the use of post-treatment antibiotic prophylaxis may be indicated in certain circumstances. CCHMC recommends it be considered for children who will have imaging until the results are known. EAU notes that it may be used after an acute episode of UTI until the diagnostic work-up is completed. EAU also recommends low-dose antibiotic prophylaxis if there is an increased risk of VUR and recurrent UTI. Antimicrobial agents recommended by both groups

include TMP, nitrofurantoin and cephalexin. CCHMC also recommends amoxicillin; EAU also recommends cefaclor.

Imaging Tests

The guideline groups agree that when imaging is indicated, an ultrasound and a cystogram should be performed. Recommendations regarding the populations in which imaging should be performed, as well as the type of cystogram that should be used differ. Refer to Areas of Differences below.

Both guidelines agree that an optional evaluation for children with UTI is to perform a renal cortical (DMSA) scan. CCHMC notes that this should be an option to children with febrile UTI, especially those over the age of three. They add that a renal cortical scan should be considered if identification of acute pyelonephritis or renal scarring will affect management decisions in febrile UTI.

Follow-Up/Prevention of Recurrence

CCHMC provides recommendations specifically pertaining to follow-up procedures, noting that routine follow-up urine testing after an episode of UTI is not recommended. They also recommend that follow-up assessment for expected clinical response occur after 48-72 hours of antimicrobial therapy. Maintaining a high index of suspicion for recurrent UTI is also emphasized by CCHMC. EAU does not provide detailed information regarding follow-up, but does note that if renal scarring is detected the patient will need careful follow-up by a pediatrician.

Areas of Differences

Antibiotic Therapy

Recommendations differ regarding duration of oral antibiotic therapy for the management of non-severe, uncomplicated UTI. EAU recommends a course of 5 to 7 days. CCHMC, in contrast, recommends a minimum course of 7 to 14 days.

Imaging Tests

While both groups agree that imaging should be performed after first UTI in boys, imaging recommendations for girls differ. CCHMC provides its criteria for imaging in girls according to age, clinical presentation, and the number of episodes of UTI, while EAU's criteria is based solely on the number of episodes of UTI. CCHMC recommends that girls with a **first** UTI that are < 36 months of age (they note that this age cutoff may vary) or age 3-7 years with fever >38.5°C (101.3°F) should undergo imaging. EAU recommends investigational imaging be undertaken after two UTI episodes in girls.

When imaging is indicated, the guidelines are in agreement that a US and cystogram should be performed. Recommendations regarding the type of cystogram that should be performed, however, differ. EAU recommends VCUG for all children in whom imaging is indicated. CCHMC, in contrast, recommends VCUG for boys and RNC *or* VCUG in girls. They note that if an RNC has been ordered and

if there are significant US abnormalities, the radiology staff physician will ask to substitute a VCUG for the RNC at that appointment.

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